Subpart E—Quality Factors for Infant Formulas

§ 106.96 Requirements for quality factors for infant formulas.

The regulations set forth in this subpart define the minimum requirements for quality factors for infant formulas:

(a) An infant formula shall meet the quality factor of normal physical growth.

(b) A manufacturer of an infant formula that is not an eligible infant formula shall demonstrate that a formula supports normal physical growth in infants when fed as a sole source of nutrition by conducting, in accordance with good clinical practice, an adequate and well-controlled growth monitoring study of the infant formula that:

(1) Is no less than 15 weeks in duration, enrolling infants no more than 2 weeks old at time of entry into the study;

(2) Includes the collection and maintenance of data on formula intake and anthropometric measures of physical growth, including body weight, recumbent length, head circumference, average daily weight increment, and average daily recumbent length increment;

(3) Includes anthropometric measurements made at the beginning and end of the study, and at least four additional measurements made at intermediate time points with three of the six total measurements made within the first 4 weeks of the study and three measurements made at approximately 4-week intervals over the remaining 11 weeks of the study;

(4) Compares the anthropometric data for the test group to a concurrent control group or groups at each time point and compares the anthropometric data for each infant (body weight for age, body length for age, head circumference for age, and weight for length) in the test group and the control group to the 2009 CDC growth charts, which are incorporated by reference at § 106.160; and

(5) Compares the data on formula intake of the test group with a concurrent control group or groups and a scientifically appropriate reference.

(c) The Food and Drug Administration will exempt a manufacturer from the requirements of paragraph (b) of this section, if:

(1) The manufacturer requests an exemption and provides assurances, as required under § 106.121(b), that the changes made by the manufacturer to an existing infant formula are limited to changing the type of packaging of an existing infant formula (e.g., changing from metal cans to plastic pouches); or

(2) The manufacturer requests an exemption and provides assurances, as required under § 106.121, which demonstrate that:

(i) An alternative method or study design that is based on sound scientific principles is available to show that the formula supports normal physical growth in infants when the formula is fed as the sole source of nutrition;

(ii) The change made by the manufacturer to an existing formula does not affect the ability of the formula to support normal physical growth; or

(iii) The manufacturer markets a formulation in more than one form (e.g., liquid and powdered forms) and the quality factor requirements are met by the form of the formula that is processed using the method that has the greatest potential for adversely affecting nutrient content and bioavailability.

(d) A manufacturer of a new infant formula that is not an eligible infant formula shall, in accordance with § 106.100(p)(1), make and retain records demonstrating that the formula meets the quality factor of normal physical growth.

(e) An infant formula shall meet the quality factor of sufficient biological quality of protein.

(f) A manufacturer of an infant formula that is not an eligible infant formula shall demonstrate that a formula meets the quality factor of sufficient biological quality of protein by establishing the biological quality of the protein in the infant formula when fed as the sole source of nutrition using an appropriate modification of the Protein Efficiency Ratio (PER) rat bioassay described in the ''Official Methods of Analysis of AOAC International,'' 18th ed., sections 45.3.04 and 45.3.05, ''AOAC Official Method 960.48

Protein Efficiency Ratio Rat Bioassay,'' which is incorporated by reference at §106.160. The PER rat bioassay shall be conducted on a formula and the results evaluated prior to the initiation of a growth monitoring study of the formula that is required under paragraph (b) of this section.

(g) The Food and Drug Administration will exempt a manufacturer from the requirements of paragraph (f) of this section, if:

(1) The manufacturer requests an exemption and provides assurances as required under §106.121(g) that the changes made by the manufacturer to an existing infant formula are limited to changing the type of packaging of an existing infant formula (e.g., changing from metal cans to plastic pouches); or

(2) The manufacturer requests an exemption and provides assurances, as required under §106.121(h), that demonstrate that the change made by the manufacturer to an existing formula does not affect the bioavailability of the protein.

(3) The manufacturer requests an exemption and provides assurances, as required under §106.121(i), that demonstrate that an alternative method to the PER that is based on sound scientific principles is available to demonstrate that the formula supports the quality factor for the biological quality of the protein.

(h) A manufacturer of a new infant formula that is not an eligible infant formula shall, in accordance with §106.100(q), make and retain records demonstrating that the formula meets the quality factor of sufficient biological quality of protein.

(i) The following provisions for requirements for quality factors apply only to an ''eligible infant formula'' as defined in §106.3:

(1) An eligible infant formula that fulfills one or more of the following criteria meets the quality factor of normal physical growth:

(i) The scientific evidence on such infant formula meets the requirements of paragraph (b) of this section that apply to infant formula that is not an eligible infant formula;

(ii) The scientific evidence on such infant formula meets the following provisions:

(A) The evidence is an adequate and well-controlled growth study, conducted in accordance with good clinical practice, to determine whether an infant formula supports normal physical growth in infants when the formula is fed as the sole source of nutrition;

(B) The growth study is no less than 4 months in duration, enrolling infants no more than 1 month old at time of entry into the study;

(C) The growth study collects from the study subjects data on anthropometric measures of physical growth, including body weight, recumbent length, head circumference, and average daily weight increment, and plots the data on the following charts from ''Physical Growth: National Center for Health Statistics Percentiles'' for body weight, body length, and head circumference, which are incorporated by reference at §106.160:

(*1*) *Figure 1*. Length by age percentiles for girls aged birth–36 months (p. 609);

(*2*) *Figure 2*. Length by age percentiles for boys aged birth–36 months (p. 610);

(*3*) *Figure 3*. Weight by age percentiles for girls aged birth–36 months (p. 611);

(*4*) *Figure 4*. Weight by age percentiles for boys aged birth–36 months (p. 612);

(*5*) *Figure 5*. Head circumference by age percentiles for girls aged birth–36 months (p. 613);

(*6*) *Figure 6*. Weight by length percentiles for girls aged birth–36 months (p. 613);

(*7*) *Figure 7*. Head circumference by age percentiles for boys aged birth–36 months (p. 614); and

(*8*) *Figure 8*. Weight by length percentiles for boys aged birth–36 months (p. 614); and

(D) The growth study collects anthropometric measurements at the beginning of the growth study, at 2 weeks, at 4 weeks, at least monthly thereafter, and at the conclusion of the study; or

(iii) The scientific evidence on such infant formula otherwise demonstrates that such formula supports normal physical growth.

(2) An eligible infant formula that fulfills one or more of the following criteria meets the quality factor of sufficient biological quality of the protein:

(i) The scientific evidence on such infant formula meets the requirements of paragraph (f) of this section that apply to infant formula that is not an eligible infant formula;

(ii) The scientific evidence on such infant formula is a study that establishes the biological quality of the protein in an infant formula by demonstrating that the protein source supports adequate growth using the Protein Efficiency Ratio (PER) rat bioassay described in sections 45.3.04 and 45.3.05 of the ''Official Methods of Analysis of the Association of Official Analytical Chemists,'' 16th ed., which are incorporated by reference at §106.160; or

(iii) The scientific evidence on such infant formula otherwise demonstrates that the protein in such infant formula is of sufficient biological quality.

(3) The manufacturer of an eligible infant formula may, not later than November 12, 2015, submit a petition to the Food and Drug Administration under §10.30 of this chapter that:

(i) Demonstrates that such formula fulfills one or more of the criteria in paragraph (i)(1) of this section; or

(ii) Demonstrates that such formula fulfills one or more of the criteria in paragraph (i)(2) of this section.

(4) A petition filed under paragraph (i)(3) of this section shall address only one infant formula formulation and shall contain all data and information relied upon by the manufacturer to demonstrate that such formulation fulfills one or more of the criteria in paragraph (i)(1) or in paragraph (i)(2) of this section. A manufacturer may combine petitions submitted under paragraphs (i)(3)(i) and (i)(3)(ii) of this section that relate to the same formulation.

(5) The manufacturer of each eligible infant formula shall make and retain, in accordance with §106.100(p)(2), records to demonstrate that such formula supports normal physical growth in infants when fed as the sole source of nutrition and shall make and retain, in accordance with §106.100(q)(2), records to demonstrate that that the protein in such infant formula is of sufficient biological quality. The records required by this paragraph shall include all relevant scientific data and information and a narrative explanation of why the data and information demonstrate that the formula supports normal physical growth and a narrative explanation of why the data and information demonstrate that the protein in such infant formula is of sufficient biological quality.

[79 FR 8059, Feb. 10, 2014, as amended at 79 FR 33071, June 10, 2014]

Subpart F—Records and Reports

§ 106.100 Records.

(a) Every manufacturer of infant formula shall maintain the records specified in this regulation in order to permit the Food and Drug Administration to determine whether each manufacturer is in compliance with section 412 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 350a)).

(b) The manufacturer shall maintain all records that pertain to food-packaging materials subject to §174.5 of this chapter and that bear on whether such materials would cause an infant formula to be adulterated within the meaning of section 402(a)(2)(C) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 342(a)(2)(C)).

(c) The manufacturer shall maintain all records that pertain to nutrient premix testing that it generates or receives. Such records shall include, but are not limited to:

(1) Any results of testing conducted to ensure that each nutrient premix is in compliance with the premix certificate and guarantee and specifications that have been provided to the manufacturer by the premix supplier, including tests conducted when nutrients exceed their expiration date or shelf life (retest date).

(2) All certificates and guarantees given by premix suppliers concerning the nutrients required by section 412(i) of the Federal Food, Drug, and Cosmetic Act and §107.100 of this chapter.

(d) The premix supplier shall maintain the results of all testing conducted to provide all certificates and